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ACL Research Retreat IX Summary Statement: The Pediatric Athlete, March 17–19, 2022; High Point, North Carolina

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The ACL Research Retreat IX was held March 17–19, 2022, at High Point University in High Point, North Carolina. This meeting brought together clinicians and researchers to present and discuss recent research advances across the entire anterior cruciate ligament (ACL) injury continuum to include primary, secondary, and tertiary risk identification, outcomes, and prevention strategies. An illustration of this continuum was provided in the 2019 "Anterior Cruciate Ligament Research Retreat VIII Summary Statement."[1] The unique focus of the current meeting was the pediatric athlete (aged 8 to 18 years). We have seen rising numbers of ACL injury diagnoses and ACL reconstructions (ACLRs) in this age group over the past 3 decades,[2–5] and these increases were substantially greater than in older age groups. Epidemiologic studies consistently indicated that few ACL injuries occurred before the age of 10 and then they increased rapidly and steadily from age 11 to 17 years,[2,6–8] when girls developed a 3-fold to 4-fold greater risk than similarly trained boys.[9,10] Moreover, young girls were more likely to incur a second ACL injury soon after returning to sport participation.[11–14] Thus, evidence-based screening and strategies to mitigate the risk of both primary and secondary injuries and improve long-term outcomes are critically needed in this age group. Because many risk factors associated with ACL injury develop or change during physical maturation, we sought to understand the maturational biopsychosocial factors that contribute to primary and secondary ACL injuries and affect both short-term and long-term joint health.

To provide a framework for the meeting and our discussions, we introduced a theoretical risk factor model (Figure) to connect the initial risk of ACL injury to long-term knee-joint–related disability, such as posttraumatic osteoarthritis (PTOA). As the model suggests, at several key time points, targeted screenings and interventions may mitigate the risk of primary ACL injury and secondary ACL injury and the subsequent risk of PTOA. To that end, ACL Research Retreat IX featured 3 keynote presentations and 42 platform presentations that provided new insights to inform ACL injury risk and prevention across this continuum.

KEYNOTE SUMMARIES

The first keynote from Matthew Fisher, PhD, of North Carolina State University and the University of North Carolina at Chapel Hill, addressed basic science research seeking to characterize ACL structure and functional biomechanics during growth and development. Highlights from this keynote included the following:

- The ACL undergoes considerable tissue-level and subtissue-level changes during skeletal growth, which could affect the injury, diagnosis, effectiveness of treatment, and subsequent degenerative changes.
- Translational animal models can aid in expanding basic science knowledge of the ACL, such as the changing subtissue-level mechanical behavior of the ACL during skeletal growth.[15,16]
- Given the difficulty of assessing ACL function in vivo in human participants, a translational animal model can be used to study age-specific and sex-specific mechanics of the ACL and knee joint.[17]

In the next keynote, Laura Schmitt, PT, MPT, PhD, of The Ohio State University, discussed optimizing knee rehabilitation outcomes and return-to-play criteria after ACLR in adolescents. She focused on the need for improved methods of determining the functional capacity of the injured limb post-ACLR:

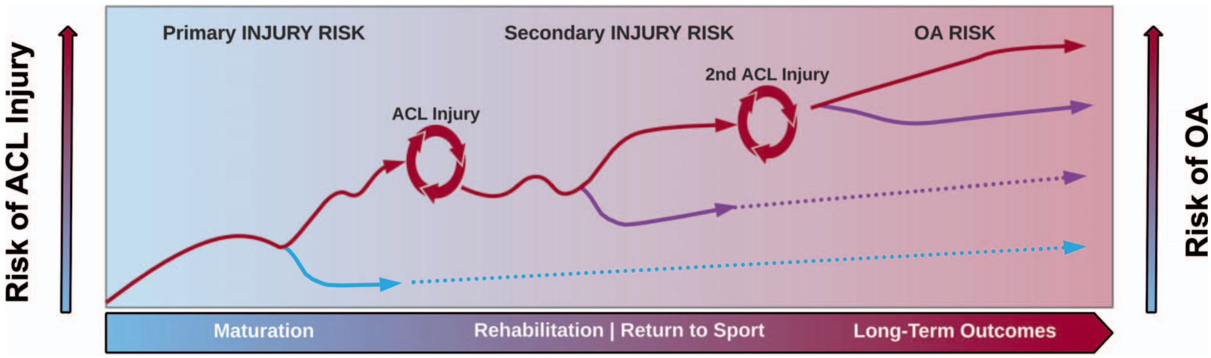

Figure. Anterior cruciate ligament (ACL) risk-factor model. Solid red lines represent theoretical paths of ACL injury and osteoarthritis (OA) with respect to relative time (x axis) and increasing risk of injury/disease (y axis). Arrowed circles indicate a combination of risk factors and inciting events that result in ACL injury. Blue lines represent a potential change in primary risk if the appropriate intervention occurs during physical maturation before a primary injury. Purple lines indicate a potential change in the secondary injury or posttraumatic OA risk with evidence-based rehabilitation strategies that target primary and secondary risk factors and restore full functional capacity.

- In addition to an increased risk of second injury and decreased chance of returning to the preinjury sport and performance participation level, young, active individuals are experiencing poor health outcomes after ACL injury or ACLR. These include compositional cartilage changes and persistent symptoms in the first 1 to 2 years after reconstruction. Also, declines in physical activity participation, including less time in moderate-to-vigorous activity and fewer daily steps, are commonplace in young individuals post-ACLR.
- To change these outcomes for young individuals post-ACLR, we need to begin with the end in mind. Maximizing quadriceps strength early after ACLR and normalizing joint-loading patterns appear critical for long-term joint health. The use of objective measures driven by sex-normative and age-normative values to benchmark strength, function, and performance can inform the rehabilitation progression and return-to-sport decisions.[18] Further, incorporating *physical literacy*[19] (the ability, confidence, and desire to engage in physical activity for life[20]) into rehabilitation has the potential to promote positive long-term health outcomes.

In the final keynote, Theodore Ganley, MD, of Children's Hospital of Philadelphia, addressed optimizing surgical techniques and outcomes for the immature knee. Highlights from this keynote included the following:

- In discussing the current state of best practices in the care of the pediatric patient with an ACL injury, Dr Ganley focused on physeal-sparing surgical interventions and how they may differ during physical maturation.
- In making return-to-sport decisions regarding the pediatric patient post-ACLR, no "one-size-fits-all" approach exists. These decisions require input from all stakeholders.
- For the treatment of pediatric ACL injuries, patients and parents need to be part of a shared decision-making process. This could mean changing sports or engaging in the process of reconstruction and rehabilitation. For these patients, modifying activity may not mean completely eliminating the sport but transitioning to safer practices.

PLATFORM PRESENTATION SUMMARIES

The retreat also featured 42 platform presentations that provided new insights across the ACL injury continuum and are available in this special ACL issue (doi:10.4085/1062-6050-1005.22). Platform presentations were organized around themes of ACL injury risk assessment, ACL injury risk reduction, neurocognitive factors for primary risk, neurocognitive considerations in primary and secondary risk reduction, risk considerations for individuals post-ACLR, and considerations for ACLR surgical implications and PTOA. Substantial time was provided throughout the conference for group discussion to summarize recent advances and emerging trends and identify strategic initiatives for future research. The summary of these presentations and conversations is organized by primary ACL injury, secondary ACL injury, and tertiary injury (osteoarthritis [OA]). This summary is not designed to be a sweeping consensus but rather an executive summary of the key findings and discussion highlights with the goal of encouraging and steering future research directions.

Primary ACL Injury

Our discussion of primary ACL injury covered the identification of risk factors, injury risk screening, and intervention strategies.

Identification of Risk Factors. The conference began with the presentation of a systematic review that examined the sex-specific trajectories of changing physical risk factors by chronological age and maturity status. Evidence was provided for a sequential, sex-specific development of physical risk factors that began with early sex differentiation in the trajectory of body composition, followed by leg strength and power, knee-joint anatomy and laxity, and lower extremity biomechanics.[21] These data clearly showed that body mass index (weight by stature), which has been consistently identified as an independent risk factor for ACL injury,[22–24] was a poor representation of body composition during maturation. Although body mass index increased similarly in boys and girls during the pubertal transition, the proportions of the fat mass index and fat-free mass index (FFMI) differed markedly, with boys already having a greater FFMI by age 10, and, by about the age of 13, the fat mass index increased more in girls and the FFMI more in boys. Additionally, sex-specific trajectories in ACL size (emerging at 14 years) closely followed sex-specific trajectories in thigh-muscle-mass development (emerging at 13 years), which led to discussions of ACL size and the extent to which these trajectories could be altered (ie, restraint capacity increased) during the developmental process. Research has indicated that ACL size is more strongly associated with muscle size than with other body dimensions[25,26] and was also associated with prolonged training,[27,28] particularly when training began at younger ages.[27] Despite widespread evidence of bone and tendon adaptations to increases in load, how ligamentous tissue responds to increases in training load or if the training load alone is sufficient to increase this capacity is not widely understood. The ability to positively affect ACL structure through training also has implications for developmental changes in knee-joint laxity,[21,29] an additional risk factor for ACL injury.[23,24]

Along with physical risk development, multiple authors and much conversation addressed the role of the central nervous system (CNS) in the ACL injury risk. Sensory processing, neurocognition, motor planning and execution, and psychological preparedness for activity were all examined. Work presented at the meeting provided evidence that sensory information during ACL loading may differ in lax individuals (Park-Braswell et al), suggesting that a lax ligament may have neurofunctional and neurostructural implications for knee sensorimotor control. Whereas previous investigators[30] associated a history of concussion with a risk of ACL injury, Zuleger et al supplied preliminary data for a potential central mechanism for the elevated ACL injury risk in those with a concussion history. Adolescent female athletes with a history of concussion showed reduced neural activity and concurrent connectivity alterations that indicated possible proprioceptive processing deficits. The authors of several studies offered at the meeting identified prospective neurologic factors that may have contributed to the neuromuscular control that propagates injury. Reduced knee motor coordination of a lower extremity task performed during functional magnetic resonance imaging by adolescent female athletes was associated with less activity in regions of the brain linked to visuospatial integration and working memory (Kim et al). Preliminary prospective work indicated that female adolescents who went on to tear their ACLs had greater brain activity associated with proprioceptive processing demands to coordinate bilateral knee motor control than uninjured participants (Diekfuss et al). These findings supported other CNS research into deficits in neurocognitive testing (associated with CNS function) that predicted ACL injury,[31] which led to a discussion about when we should begin to use such measures in a pediatric population. As do other physiological systems during physical maturation, the CNS undergoes structural changes.[32] Further, we understand that white matter structure and function do not mature until early adulthood.[33] Age-related differences in brain activity in a pediatric population were noted during a leg-press activity (Warren et al). Specifically, increasing age (12–17 years) was associated with less brain activity in areas involving spatial cognition, self-location, and attention.

Collectively, these investigations provided additional evidence that central factors may be important in the rapid increase in ACL injuries during the maturational process and pointed to the need for future research in this area (also see related papers in this special issue). However, although standardized neurocognitive assessment is typically much easier to perform, we need to better understand brain function during physical activity and how this may predict ACL injury. Such factors are especially apparent as behavior (neurocognitive performance) can normalize at the expense of sensorimotor neural activity compensations.[34] Attendees also expressed a desire for normative, task-based functional magnetic resonance imaging measures to reduce the requirement for a control group when identifying those with a sensorimotor neural activation strategy that poses a high injury risk. However, thus far, the neuroimaging data have been preliminary and specific to group-related or task-related contrasts. Normative data to determine a threshold of excessive or inadequate activation of specific brain regions for classifying individuals with a sensorimotor activation strategy reflecting a high injury risk is a future research objective.

Other primary risk factors centered on the concept of physical activity patterns and literacy during the physical maturational process. We must understand the timing of, types of, and changes in physical activity patterns during growth and development to establish how these factors may affect the development of high-risk biomechanical patterns associated with ACL injury. How and when physical activity may be associated with strength development and contribute to a reduction in the risk of ACL injury was also addressed.

Injury Risk Screening. Debate focused on what should be measured as part of the screening process and when screening should occur, as prioritizing cost-effective field and clinically accessible measures to evaluate risk potential is critically important. This is especially true when working with a pediatric population, in whom the patient and parent or guardian burden becomes even more significant. The consensus was that ACL injuries were rarely seen in patients younger than age 11; the risk increased incrementally thereafter until full maturity. Vital questions were when and how we should begin to assess risk in the pediatric population if we are to be most effective in preventing primary injury. The feasibility of using maturation versus age as a marker of when to begin risk assessment was considered. Given the wide age ranges at which boys and girls initiate and progress through the pubertal transition and the fact that this transition occurs 1 to 2 years later in boys, attendees agreed that maturation was a better metric than age for assessing the timing of risk development. Which maturational measure (eg, Tanner stage, age and peak height velocity, skeletal age) should be used and when assessment should begin are still unknown. However, for large-scale risk assessment, simple and noninvasive tools that relate well to physiological growth spurts (eg, height and weight measures, self-reported pubertal assessment, shoe size) were required. Another topic was how often risk should be assessed and when a child "ages out" of the need for assessment. That is, what is the appropriate interval for a follow-up risk assessment? Based on the timing and tempo of Tanner stage progression, an ideal timeframe of every 6 months was suggested, with $\leq$1 year elapsing between assessments.

Reduction in Primary ACL Injury. Changes in strength and movement biomechanics among young female athletes in response to a variety of neuromuscular training programs were presented (Ford et al, Nguyen et al). Plyometric-based neuromuscular training resulting in brain activation during a lower extremity task indicated a neural efficiency adaptation for motor coordination (Chaput et al). Beyond established neuromuscular training programs, investigations involved the manipulation of feedback through a variety of mechanisms: biofeedback focused on a specific body region (Ford et al), autonomy support (Hogg et al, Nijmeijer et al), enhanced expectancies (Hogg et al), and visual feedback (Slutsky-Ganesh et al). One group's research demonstrated that emphasizing feedback on the underlying mechanism of aberrant biomechanics (hip focused) may provide greater transfer to other sporting tasks than a more localized knee-centric approach (Ford et al). Support continues to build for understanding the role of cognitive manipulation in prevention programming and how manipulating neuromuscular training programs may result in positive neuroplastic adaptations, which may benefit longer-term motor learning, redetection, and transference.

Recognizing and appreciating the difficulty of performing large-scale prospective prevention studies, we focused on the factors that may help researchers conduct these experiments successfully. A large randomized controlled trial (Ford et al, Nguyen et al) with excellent adherence and compliance rates >90% spoke to the value of achieving rapport and a therapeutic alliance with all stakeholders, including the athletes, parents, and members of the coaching staff and club or school administrators. Others suggested that involving stakeholders to identify needs and their willingness to engage can help with rapport building and allow for a more tailored approach to intervention designs.

As during previous retreats, the concept that reducing the incidence of ACL injury may benefit from a more public health perspective was reiterated. To promote the best-practice decisions by the patient and health care provider, we must put information in stakeholders' hands. The authors of a systematic review of knowledge, attitudes, and beliefs among sport stakeholders (Hawkinson et al) reported that implementation science frameworks have the potential to identify the barriers to implementation and could be beneficial in developing programming (based on the best science) that may meet the needs of stakeholders most effectively. It is imperative that the research community disseminate information in a manner appropriate to the target audience. Although coaches and athletes may be receptive to prevention strategies, our responsibility is to make the information accessible.

Secondary ACL Injury

Regarding secondary injury, even though many of the risk factors of the primary injury persist after the initial ACL injury, the risk factors that may be unique to secondary ACL injury should continue to be refined. Given the likely interaction of multiple factors, we need to develop a model that better describes primary versus secondary injury and what cluster of variables is most critical in determining injury risk.

As with primary injury, evaluating lower extremity strength and biomechanics was a principal focus in assessing the patient's readiness to safely return to sporting activity post-ACLR. Based on a retrospective case-control design, female athletes with a lower hip-knee extensor strength ratio post-ACLR were at greater risk of ACL reinjury (Straub and Powers). Although the participants were not all youngsters, long-lasting impairments in quadriceps mitochondrial health (Davi et al) and differential patterns of muscle asymmetry (Hartshorne and Padua, Hart et al) were evident after ACL injury. Comparisons of adolescent and adult gait patterns showed that adolescents walked at slower gait speeds and displayed more-crouched gait kinematics characterized by less knee-flexion excursion (Lisee et al) but demonstrated no apparent difference in gait variability (Armitano-Lago et al). How such gait patterns may localize tibiofemoral compartment loading was considered.

The psychological readiness to return to activity was another focus of attention—specifically, the constructs of confidence and kinesiophobia. As fear is a necessary human emotion that aids in survival, attendees emphasized taking a biopsychosocial, holistic approach when studying these constructs. Challenges to the validity of assessing these in the clinic or laboratory environment and then applying the results to the activity setting were acknowledged. Ecological momentary assessment may allow clinicians and researchers to better relate the psychosocial state to the actual activity of the patient.

The concept of an individualized medicine approach to understanding the risks surrounding return to activity after a primary ACL injury was deliberated. The development of a promising machine-learning model of pediatric ACL reinjury risk was presented (Greenberg et al). Such a model has the potential to individually assess risk and provide customized methods of better directing secondary injury prevention. Similarly, a dashboard or business informatics platform approach was suggested (Kuenze et al) that would offer the clinician age-specific and sex-specific reference variables, thereby allowing more individualized decision making.

Improving and refining return-to-sport testing was a frequent topic. Although wearable activity monitoring was not directly explored at the meeting, how such physiological devices may help us to better understand cumulative physical activity and its role in injury causation was the subject of much conversation. Related was the need to comprehend the role of fatigue in return-to-play testing. Questions exist about the robustness of return-to-play testing when the athlete is in a more fatigued state, which may affect the ability to avoid further joint injury.

Tertiary Injury

The role of ACL injury, surgery, and rehabilitation in the onset and progression of PTOA was explored in multiple ways. As with the primary and secondary injury risks, the role of psychosocial measures was examined. In a younger female population (aged 13–25 years), poor psychological readiness and elevated injury-related fear after ACLR was associated with greater odds of experiencing early knee OA symptoms (Baez et al). In an adolescent ACLR population (13–17 years), at 6 to 12 months post-ACLR, 47% of patients met the criteria for early knee OA symptoms. Although this percentage was greater in adults, it merits attention from health care providers (Harkey et al) who have the potential to implement a more targeted program to minimize OA symptoms beyond the traditional return-to-play rehabilitation timeframe. The necessity of separating structural joint changes (disease) from patient-reported symptoms (illness) was cited. This perspective may help to better focus research into providing better care of the patient post-ACLR.

Another subject was how the onset and progression of OA may be modified by an intervention program. Despite substantial challenges in determining the effectiveness of such programs due to the very long-term longitudinal designs needed, such work will be helpful in identifying the types of interventions that should be tested. Interventions could include strength training, novel gait retraining, lifestyle modification, activity modification, and anxiety modification, for example. Also important is specifying appropriate criteria for inclusion in clinical trials to evaluate who will develop OA rapidly enough to assess the benefit of such changes.

SUMMARY

The incidence of ACL injuries in young athletes has increased over the last 3 decades, with girls showing the greatest increases.[2] As athletes reach their mid-teens and progress into later maturational stages, sport-related ACL injuries continue to rise. Therefore, the early to mid-teens would appear to be an optimal window for injury-prevention interventions compared with targeting the late teens and early adult years.[35] A primary take-home message from the discussions of primary risk was the importance of continued efforts to recognize the earliest onset of risk development at the individual level, so that we can determine the optimal window and targets for interventions. It is also becoming increasingly evident that we must move beyond physical risk assessment and address cognitive factors as well. Still, despite our best preventive efforts, some individuals will go on to experience ACL injuries. Attendees at this meeting identified a number of key directions for future research in the areas of primary and secondary risk-factor identification and optimizing interventions for reducing secondary injury while ensuring the best outcomes for long-term joint health. Specific to the prevention of secondary ACL injury, we need more evidence-based return-to-play criteria and a greater emphasis on psychological readiness. Psychosocial factors relative to the onset and progression of OA were considered, as were interventions for slowing or mitigating this disease. In summary, it is important to focus on the whole person and individual-level factors as ACL injury research continues to evolve.

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